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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,326	06/04/2007	Gunter Fischer	VOS0068/US	4684

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EXAMINER	
SHEN, BIN	
ART UNIT	PAPER NUMBER
1657	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,326	FISCHER ET AL.	
	Examiner	Art Unit	
	BIN SHEN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/12/2007;6/4/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The IDS received 3/12/2007, 6/4/2007, the preliminary amendment received 1/23/2007, 6/4/2007 have been entered.

Election

Applicant's election without traverse of Group I, claims 1-12, and election of species of FKBP38 for type A, P02593 for type B, Ca^{2+} for type C, in the reply filed on 7/7/2009 is acknowledged. The amended claims filed 10/13/2009 are entered and currently under examination

Claims12-20 are nonelected and thus are withdrawn from further consideration. Only claims 1-12 are presented for examination on the merits.

Benefit of priority is to 1/22/2004.

Sequence to comply

This application contains sequence disclosures on page 5, line 25, that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a((1) and (a)(2). However, this application fails to comply with one or more of the requirements of 37 C.F.R. § 1.821 through 1.825 for one or more of the reasons set forth on the attached form "Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequences And/Or Amino Acid Sequence Disclosures". Wherein attention is directed to paragraph(s) §1.82 (c) and (e). Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete.

Specification

All references to sequences in specification must include SEQ ID NOs, including Figs. No SEQ ID NOs are included for the peptide sequence on page 5, line 25.

The specification is objected to for inappropriate notation of an internet address. The specification contains an embedded hyperlink at page 19, line 2 and page 35, line 34 and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Removal of the "http://" is sufficient to comply.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 are rendered vague and indefinite by the phrase "producing" (on line 1) for the following reasons. It is confusing to use "producing" since the method is to identify/screen for modulators/effectors of an enzyme not to chemically synthesize/make the modulators/effectors.

Claims 1, 2, 5 are rendered vague and indefinite by the phrase "fragment/derivative" (on lines 5, 6 of claim 1, lines 4, 5 of claim 2, and line 2 of claim 5) for the following reasons. It is unclear as to what "fragment/derivative" is actually defining without any specific structure descriptions. The instant specification discloses that "fragment/derivative" are "truncated or modified by different methods….and exhibiting peptidyl-prolyl cis/trans isomerase activity" (see for example [0018] of instant application 20070244165) without any specific structure description. Therefore, it is unclear what specific protein structures/changes are encompassed as "fragment/derivative" for CaMAP and calmodulin.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Lam (1995).

Lam teaches a peptidyl-prolyl cis/trans isomerase assay with FKBP12.6 (a calmodulin-dependent peptidyl-prolyl cis/trans isomerase-CaMAP, page 26513, left column, 3rd full paragraph) by mixing appropriate amount of FKBP12.6 and bovine brain calmodulin in the presence or absence of drugs FK506, CsA or '818 (page 26513, left column, 3rd full paragraph, line 7 for calmodulin, line 8 for the drugs); adding an appropriate amount of peptide substrates (page 26515, Table 1); measuring CaMAP activity (page 26515, Table 1).

Therefore, Lam teaches a method for identifying an effector of a camodulin-dependent peptidyl-prolyl cis/trans isomerase: peptidyl-prolyl cis/trans isomerase assay with FKBP12.6 (a calmodulin-dependent peptidyl-prolyl cis/trans isomerase-CaMAP, page 26513, left column, 3rd full paragraph) comprising a) mixing appropriate amount of FKBP12.6 and bovine brain calmodulin in the presence or absence of drugs FK506, CsA or '818 (page 26513, left column, 3rd full paragraph, line 7 for calmodulin, line 8 for the drugs); b) adding an appropriate amount of peptide substrates (page 26515, Table 1); c) measuring CaMAP activity (page 26515, Table 1), the measuring step inherently d) detects any CaMAP effector (inhibitor or activator, steps a-d of **Claims 1, 2**).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Lam (1995).

Lam teaches a peptidyl-prolyl cis/trans isomerase assay with FKBP12.6 (a calmodulin-dependent peptidyl-prolyl cis/trans isomerase-CaMAP, page 26513, left column, 3rd full paragraph) comprising a) mixing appropriate amount of FKBP12.6 and bovine brain calmodulin in the presence or absence of drugs FK506, CsA or '818 (page 26513, left column, 3rd full paragraph, line 7 for calmodulin, line 8 for the drugs); b) adding an appropriate amount of peptide substrates (page 26515, Table 1); c) measuring CaMAP activity (page 26515, Table 1, steps a-c of **Claims 1, 2, 8**); the reaction solution contain bivalent ions Ca^{2+} ($CaCl_2$, page 26513, left column, 3rd full paragraph, line 6, **Claim 6);** the reaction solution has a pH 8 **(**page 26513, left column, 3rd full paragraph, line 5, **Claim 7);** since the enzyme assay is perform in the reaction mixture of FKBP12.6, bovine brain calmodulin and peptide substrates, thus step a) and b) are interchangeable **(Claim 9);** the reaction with peptide substrates (peptide with 4-nitroanilide, same as in Fischer 1989, page 477, Fig. 1) for the assay is detected by absorbance at 390 nm, thus the detection is carried out by spectroscopic **(Claim 10);** the reaction mixture on page 26513 (left column, 3rd full paragraph, line 5) including Tris, BSA, and drug, etc. are considered a pharmaceutically acceptable carrier or solvent **(Claim 12).**

Lam does not teach detecting the effectors as inhibitor or activator based on the CaMAP activity, fractioning the sample until the inhibitor or activator contained in the sample is present in purified form, the CaMAP is FKBP38, the calmodulin is P02593 (human); the method is a high-throughput method.

However, Lam shown that FKBP12.6 demonstrates similar enzyme activity as other CaMAP family protein (such as FKBP12) in the presence and absence of drug (page 26521, right column, lines 3-7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Lam by using the CaMAP assay to screen for effectors (step d of **Claims 1, 2, 8**) with other protein in the same CaMAP family such as FKBP38 (**Claim 4)** in

the presence of different forms of calmodulin such as P02593 (**Claim 5**) because Lam teaches a CaMAP assay with FKBP12.6 mixed with bovine brain calmodulin and suggests that FKBP12.6 demonstrates similar enzyme as other CaMAP family protein in the presence and absence of drug. One would have been motivated to make the modification because Lam et al. specifically described the peptidyl-prolyl cis/trans isomerase assay with FKBP12.6 and suggest that CaMAP family protein shares similar enzyme activity, and would reasonably have expected success in view of Lam's teaching to screen effectors for other CaMAP family protein such as FKBP38.

Regarding **claims 3, 11**, a person of ordinary skill in the art, upon reading the reference, would also have recognized the desirability of improving the method taught by Lam by fractioning the sample tested for effectors until the inhibitor or activator contained in the sample is present in purified form and apply the screening method in a high-throughput method for automation to improve the screening efficiency because a person of ordinary skill has good reason to pursue the known options within his/her technical grasp with anticipated success, thus the purification of the inhibitor/activator and the high-throughput application of the screen method is likely the product not of innovation but of ordinary skill and common sense.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Art of Record:

Fisher et al. (1989) teaches a peptidyl-prolyl cis/trans isomerase assay (PPIase).

Certain papers related to this application may be submitted to Art Unit 1657 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

B Shen
Art Unit 1657

/Karen Cochrane Carlson/

Primary Examiner, Art Unit 1656